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Synergistic Effects of Polycyclic Hydrocarbons and Nitrosamines in Pulmonary Carcinogenesis. Potential Repressors of Metabolic Activation of Nitrosamines.

The pulmonary syncarcinogenic effect of 3-methylcholanthrene (MC) and dimethylnitrosamine (DMN) in rats and mice suggests that the lung cancer incidence of smokers is due to synergism between carcinogenic hydrocarbons and nitrosamines present in the smoke, rather than to the hydrocarbons alone. Epidemiological findings indicate that roofing workers, exposed to the inhalation of enormously higher levels of benzo(a)pyrene than are even heavy smokers, have a lung cancer incidence not significantly higher than the general population.

The enzymological study of the mechanism of hydrocarbon-nitrosamine synergism is being continued by determining arylhydrocarbon hydroxylase (AHH), DMN-demethylase, epoxide hydrase and glutathione-S-epoxide transferase activities following acute and chronic administration of MC and DMN. There is firm evidence that pulmonary epoxide hydrase activity is depressed by DMN. The effect on epoxide hydrase appears to be dose-dependent, in accord with the existence of two DMN-demethylase isoenzymes. There is generally substantial difference in all these enzyme responses in AHH-inducible and -repressible mouse strains.

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